Polio eradication: What can we learn from analysis?

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Topics

- Role of risk/benefit/cost analysis
- Key uncertainties
- Insights from efforts to date

Perspective

- "All decisions are based on models… and all models are wrong"

  John Sterman, 2002

- "All models are wrong but some are useful"

  George Box, 1979

- Mental models are particularly problematic (assumptions not clear and transparent), mathematical models very useful

Risk Analysis

- Mathematical modeling tools that can help us:
  - better understand complex problems, including what we do and don't know
  - make assumptions clear and transparent
  - put questions in context and weigh trade-offs
  - grapple with questions of science and our (individual and societal) values and preferences
  - ask better questions, hopefully get better answers
  - find areas of agreement and disagreement
- Better than the alternative
- Most valuable when the stakes of decisions very high

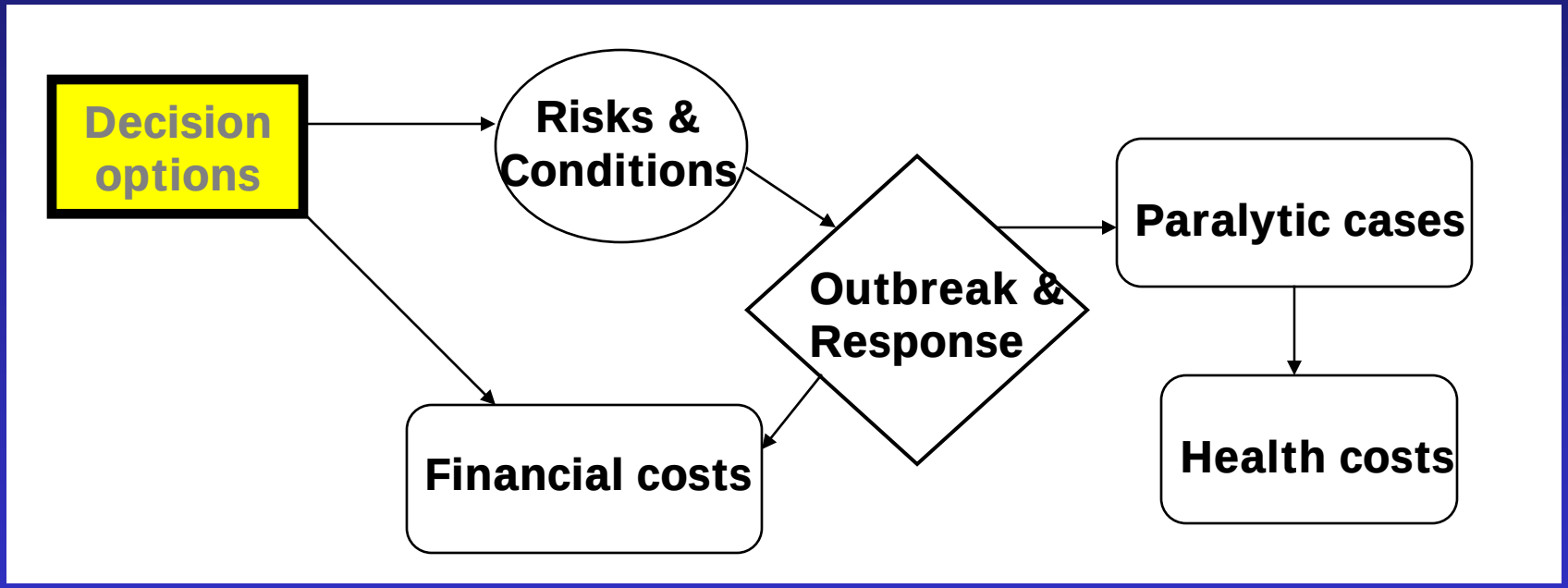
Value recognized by GPEI

- **Objective 3 of Strategic Plan 2004-2008: Develop Products for the Global OPV Cessation Phase**

  "… the focus of this area of work has been to first define and quantify the risks of paralytic poliomyelitis following global certification, due to either the continued use of OPV or the continued handling of wild polioviruses or potentially infectious materials. An agenda of research and programme work was established to inform this risk framework and to study potential strategies for their mitigation. Particular attention was given to defining the financial costs, economic implications, technical and regulatory feasibility, and operational practicality of each potential strategy."

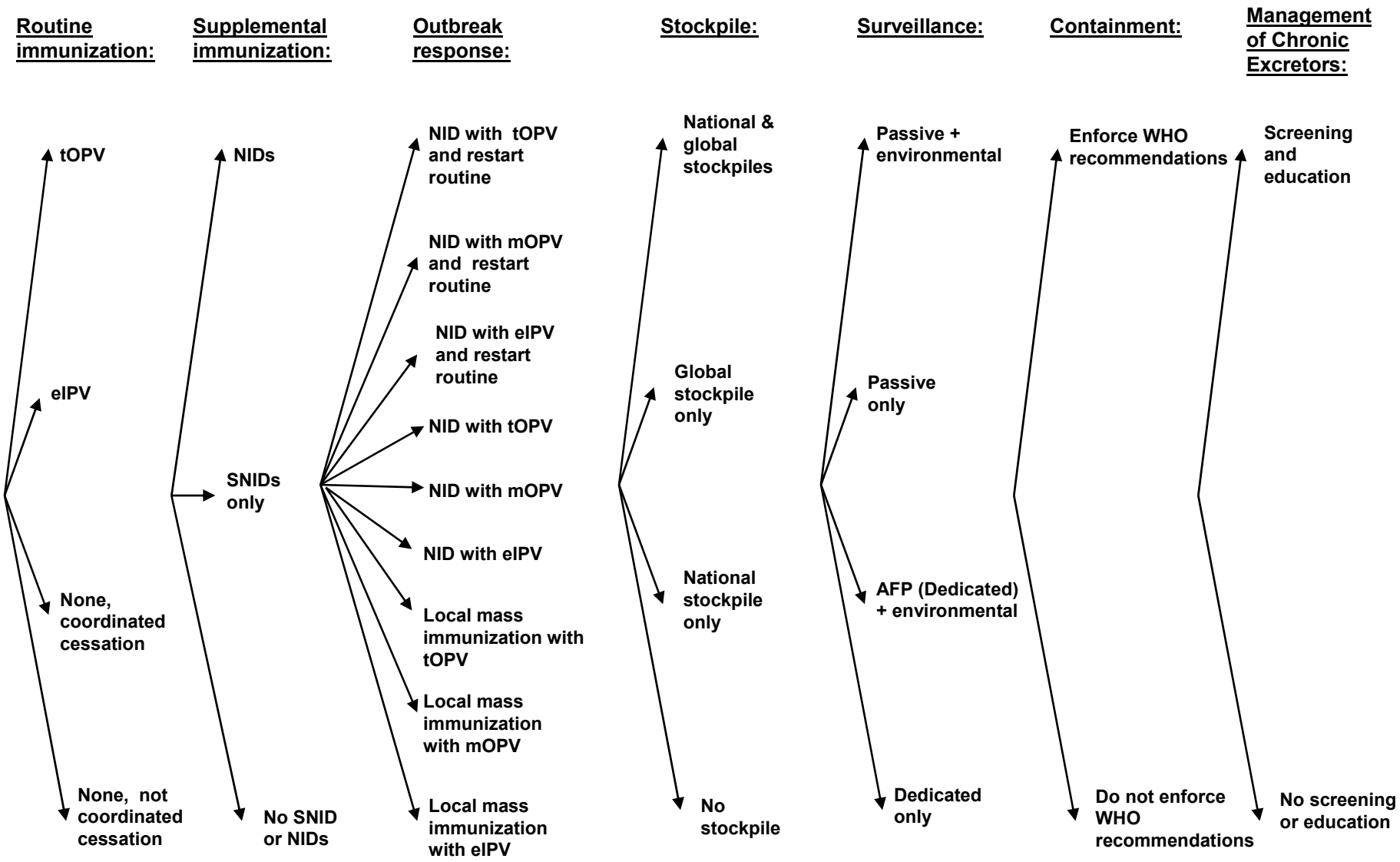
Decision options

Many options and variability among countries in preferences, resources, and thus options → stratify countries by income level



Sangrujee NK, Duintjer Tebbens RJ, Cáceres VM, Thompson KM. "Policy Decision Options During the first Five Years Following Certification of Polio Eradication." Medscape General Medicine 2003(December 19);5(4). (Available at: http://www.medscape.com/viewarticle/464841.

Major decision options for all countries – first five years after certification



Faster response is better

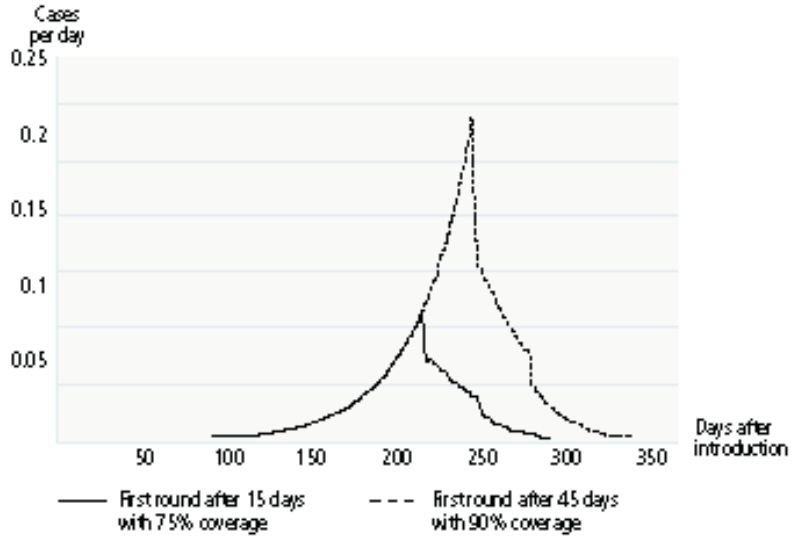
Polio outbreak response: the faster, the better…

In line with the standing recommendations for outbreak response by the Advisory Committee on Polio Eradication (ACPE) (see page 2), mathematical modelling predicts that a rapid, large-scale immunization response is preferable to a delayed response. Exploring the trade-offs between time and coverage, mathematical modelling suggests that an initial quick response with medium coverage (above 70%) is more beneficial in controlling an outbreak than a delayed activity with higher coverage, as long as the initial rapid response is followed by two, large-scale campaigns attaining high coverage (at least >90%).

See figure on right: in a hypothetical outbreak in a low income country of 10 million people, implementing a first round with 75% coverage 15 days after the onset of the first paralytic case leads to 5 cases, compared to 11 cases if the first round occurs 45 days after the onset of the first paralytic case, but attains 90% coverage.

Rapid response translates into a lower number of cases

Main assumptions: 10 million people, low-income country, no SIAs in the previous 5 years, 50% routine OPV3 coverage, R0=10, AFP surveillance, 2nd and 3rd rounds cover 90% of under lives, all rounds use mOPV



Adapted from Kim T Thompson and Radboud Duintjer Tebbens

Thompson KM, Duintjer Tebbens RJ, Pallansch MA. Evaluation of response scenarios to potential polio outbreaks using mathematical models. Risk Analysis 2006;26(6):1541-1556.

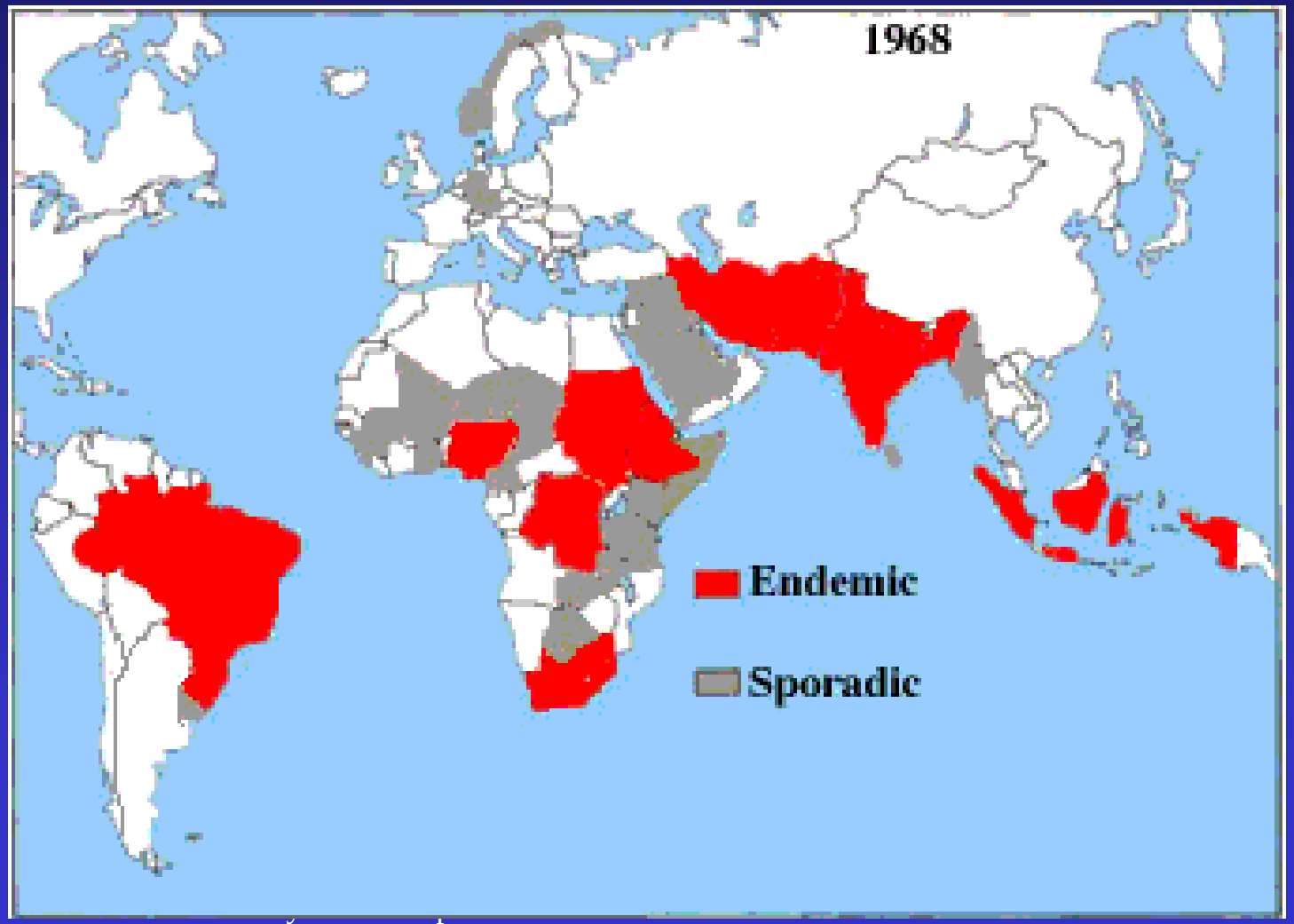
Eradication vs. Control

Thompson KM, Duintjer Tebbens RJ. Eradication versus control for poliomyelitis: An economic analysis. The Lancet 2007;369(9570):1363-71.

- **Not possible to "effectively control" (i.e., achieve low cases) at low costs**
- **Eradication requires paying large short-term costs to get long-term benefits**
- **Failure to finish eradication means real opportunity costs to other programs**
- **The sooner we finish polio eradication the better economically, wavering is costly**
- **Comparisons to only other disease eradicated to date (smallpox) must be put into context**

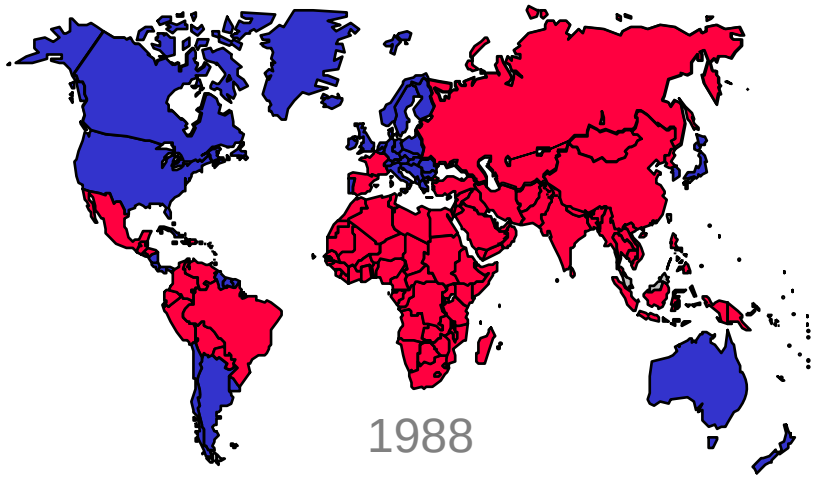
Smallpox eradication (1968-1979)

- World Health Assembly resolved to eradicate smallpox in 1958 (WHA.11.54)
- At launch of Intensified Smallpox Eradication Programme in 1967 smallpox was endemic in 31 countries with approximately 977 million people living in endemic countries
- Smallpox: 1 serotype, took 20 years to eradicate starting from 1958, much work done before 1958



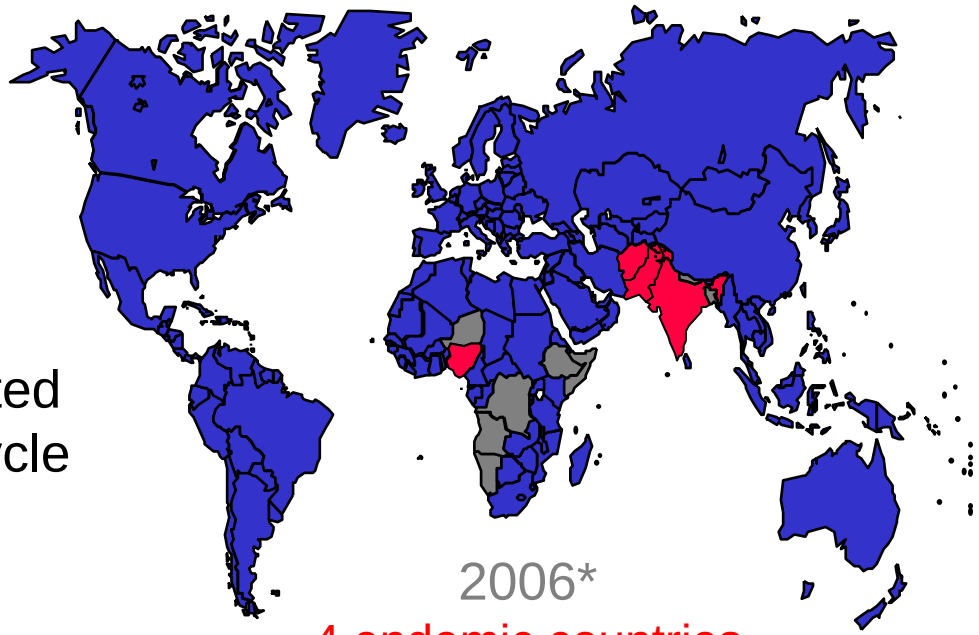
Source: http://www.microbiologybytes.com/tutorials/Pox/Pox16.html

Polio Eradication Initiative



1988

- 125 endemic countries
- 4.5 billion people



2006*

4 endemic countries

reinfected countries

Polio eradication programme started relatively much earlier in the lifecycle of the disease (compared to smallpox), nonetheless some countries did not start polio vaccination until 1999-2000

Key uncertainties - address with policies

- How will we respond to an outbreak if one occurs following WPV disruption?
- Will countries actually coordinate post-WPV disruption actions?
- How will we respond to an outbreak if one occurs after OPV cessation?
- How cheaply can we produce IPV for global routine use?
- Can we reach/maintain (high) routine coverage goals in developing countries (if not during eradication, then when and how)?
- Will we successfully maintain surveillance and long-term containment?

Key uncertainties – address with studies

- How quickly does immunity wane from various types of exposure to polioviruses?
- Can IPV interrupt transmission in the event of an outbreak?
- What production or delivery optimization might lower costs of IPV for global routine use?
- Can we develop effective antivirals and get them accepted for global use?

Key uncertainties – have to live with these

- When and where will future outbreaks occur?
  - Risks NOT zero, so we have to deal with uncertainties about the potential for reintroductions (unintentional and intentional)
  - Relatively low risks for individual countries (varies by population size, conditions, policies)
  - Global risk motivates response planning and stockpile maintenance
    - "Combining all of the risk estimates with global population forecasts suggests an approximately 50 to 100% chance of at least one outbreak during the first 20 years after global OPV cessation" (Duintjer Tebbens RJ, Pallansch MA, Kew OM, Cáceres VM, Jafari H, Cochi SL, Sutter RW, Aylward RB, Thompson KM. Risks of paralytic disease due to wild or vaccine-derived poliovirus after eradication. Risk Analysis 2006;26(6): 1471-1505.)
    - For a policy of OPV cessation after eradication of wild polioviruses, risks of cVDPVs dominate in the first 3 years – using OPV is a real risk

Example

- Suppose there are 50 independent ways that an accident can occur in a given year and managers can reduce the annual probability of each way occurring to 0.001. Prob of no accidents in 1 year:
  - $P = (1-.001)^{50} = 0.95$
- Prob of no accidents in 10 years:
  - $P = [(1-.001)^{50}]^{10} = 0.61$
- Prob of at least one accidents in 10 years:
  - $P = 1-[(1-.001)^{50}]^{10} = 0.39$

Key uncertainties – have to live with these

- "Silent" circulation is possible: if we can't see it, is it there? How long can virus circulate undetected?
- People will behave differently than we expect, what will they do?
- The virus will continue to change and new variants (potentially engineered) will always be possible
- We will never know everything that we might want to know…

Overall insights

Results of risk analyses so far reveal that:

- Risks will never be zero, we should manage them constantly and vigilantly
- Perceived risk of bioterrorism might drive high-income country preferences to continue expensive IPV vaccination while low- and middle-income countries might prefer to stop vaccination
- Eradication promises the best outcomes (costs and cases), assuming that we can achieve it, because of OPV-associated risks
- Must develop and maintain aggressive response plans and stockpile
- Plan B (control?) is expensive and never stops, we need to seriously consider the costs (health and $)